Citation:

Silvera SA, Jain M, Howe GR, Miller AB, Rohan TE. Glycaemic index, glycaemic load and ovarian cancer risk: A prospective cohort study. *Public Health Nutr.* 2007 Oct; 10(10): 1,076-1,081. Epub 2007 Mar 2.

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Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine ovarian cancer risk in association with glycemic index (GI) and glycemic load (GL), and intake of dietary carbohydrate and sugar.

Inclusion Criteria:

49,613 Canadian women enrolled in the National Breast Screening Study (NBSS) who completed a self-administered food-frequency questionnaire (FFQ) between 1980 and 1985.

Exclusion Criteria:

- Women with extreme energy intake values
- Women with prevalent ovarian cancer at baseline
- Women who had undergone a bilateral oophorectomy prior to enrolment in the study.

Description of Study Protocol:

Recruitment

- 89,835 women aged 40 to 59 years were recruited into the Canadian National Breast Screening Study (NBSS) between 1980 and 1985 from the general Canadian population by various means, including personal invitation by letter, group mailings to employees of large institutions and to members of professional associations, advertisements in newspapers and public service announcements on radio and television
- Women enrolled in the NBSS were randomized to either the screening arm or the control arm, and were followed up to assess rates of referral for screening, rates of detection of

breast cancer from screening and from community care, nodal status, tumor size and rates of death from all causes and from breast cancer.

Design

- Prospective cohort of 49,613 Canadian women enrolled in the National Breast Screening Study (NBSS) who completed a self-administered FFQ between 1980 and 1985
- Linkages to national mortality and cancer databases yielded data on deaths and cancer incidence, with follow-up ending between 1998 and 2000
- Data from the FFQ were used to estimate overall GI and GL, and Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between energy-adjusted quartile levels of GL, overall GI, total carbohydrates, total sugar and ovarian cancer risk.

Dietary Intake/Dietary Assessment Methodology

- Starting in 1982 (i.e., after some participants had completed their scheduled visits to the screening centers), a self-administered FFQ was distributed to all new attendees at all screening centers and to women returning to the screening centers for re-screening. The FFQ sought information on usual portion size and frequency of consumption of 86 food items, and included photographs of various portion sizes to assist respondents with quantifying intake
- A comparison between the self-administered questionnaire and a full interviewer-administered questionnaire, which has been subjected to both validity and reliability testing and used in a number of epidemiological studies, revealed that the two methods gave estimates of intake of the major macronutrients and dietary fiber that strongly correlated with each other (correlation coefficients ranged from 0.47 for cholesterol to 0.72 for vegetable protein; for dietary fiber, the correlation coefficient was 0.70
- A total of 49,613 dietary questionnaires were returned and available for analysis.

Statistical Analysis

- Cox proportional hazards models (using age as the time scale) were used to estimate hazard ratios (HRs) and 95% CIs for ovarian cancer risk in association with energy-adjusted quartile levels of GL, overall GI and total carbohydrate and total sugar intake; energy adjustment was performed using the residual method
- To test for trend, the median value of each quartile level was fitted as an ordinal variable in the risk models, and evaluated the statistical significance of the coefficient using the Wald test. The associations overall and within strata defined by menopausal status were examined
- Tests for interaction were based on likelihood ratio tests comparing models with and without product terms representing the variables of interest. Use of the lifetest procedure in SASw showed that the proportional hazards assumption was met in this data set. All analyses were performed using SAS version 9 (SAS Institute)
- All statistical tests were two-sided, and P-values less than 0.05 were considered to be statistically significant.

Data Collection Summary:

Timing of Measurements

- Canadian National Breast Screening Study conducted between 1980 and 1985
- Follow-up ended between 1998 and 2000, mean follow-up of 16.4 years

- FFQ distributed to participants starting in 1982.

Dependent Variables

Ovarian cancer risk.

Independent Variables

- Glycemic index
- Glycemic load
- Dietary carbohydrate intake
- Dietary sugar intake.

Description of Actual Data Sample:

- *Initial N:* 49,613 women
- *Attrition (final N):* 48,776
- *Age:* 40 to 59 years
- *Location:* Canada.

Summary of Results:

Key Findings

- GI and total carbohydrate and sugar intakes were not associated with ovarian cancer risk in the total cohort
- GL was positively associated with a 72% increase in risk of ovarian cancer (HR=1.72, 95% CI: 1.13 to 2.62, P=0.01) and the magnitude of the association was slightly greater among post-menopausal (HR=1.89, 95% CI: 0.98 to 3.65, P=0.03) than among pre-menopausal women (HR=1.64, 95% CI: 0.95 to 2.88, P=0.07).

Author Conclusion:

Dietary GL is associated with an increase in the risk of ovarian cancer.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes

2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	???